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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,030	BENOIT ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *3-6,8,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) *1,2,7 and 9-19* is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *March 17, 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *August 30, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *BLAST 2 Sequence Results*.

DETAILED ACTION

This Office Action is a response to Applicant's Election filed August 8, 2006.

Claims 1-21 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 7, and 9-19, drawn to a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide, in the reply filed on September 18, 2006 is acknowledged. The traversal is on the ground(s) that the MPEP § 803.04 states, "in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction". Applicants contend that here, there are six overlapping sequences corresponding to SEQ ID NOs: 2-7, and a seventh sequence consisting of SEQ ID NO:9.

This traversal and contention have been fully considered but are not found persuasive because although the MPEP states that up to 10 sequences are considered reasonable, such guidelines were issued in 1996, and the size of the nucleotide sequence databases has doubled approximately every six months since then. Thus, the number of returned hits for nucleotide sequence searches has expanded dramatically since the time these guidelines were issued. Furthermore, in addition to

the voluminous size of such databases, the context in which the sequences appears must also be examined, that is, each potential reference must be read and analyzed to determine if it contains one of the 5 sequences recited in claim 1. When this is considered in light of the fact that the claims read on fragments of each of the sequences recited in claim 1, or on polynucleotides that hybridize with any one of the sequences recited in claim 1, such a search may return many thousands of polynucleotide hits, each of which must be further considered as to whether it would specifically induce expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide within the claimed context. In light of these many variables, this is considered to constitute a serious burden.

Applicants also argue that the sequences recited encompass overlapping sequences derived from the same complete sequence, namely the human CARP gene. Applicants contend that a search for the smallest fragment of the overlapping fragments claimed would reveal all prior art related to each of SEQ ID NOs: 2-7.

This argument and contention has been fully considered but is not found persuasive. It is noted that SEQ ID NO:2 consists of the human CARP promoter, while SEQ ID NOs: 3-7 consists of smaller fragments of the human CARP promoter (for example, -2702/+38, -2108/+38, -2011/+38, -1543/+38, and -772/+38, respectively). While it is recognized that SEQ ID NO:7, the smallest fragment of the overlapping fragments, is found in each of SEQ ID NO: 2-6, and art against SEQ ID NO:7 will reveal prior art related to each of SEQ ID NOs: 2-7, the same does not hold true for art relating to SEQ ID NOs: 2-6 against SEQ ID NO:7. More specifically, a search for each of SEQ

ID NOs: 2-6 would not necessarily reveal art against SEQ ID NO:7. As detailed in the previous restriction requirement mailed July 19, 2006, the polynucleotides of SEQ ID NO:2-7 are different molecules with different chemical and physical structures so that independent searches of the prior art would be required that would constitute a serious burden on the Examiner. As further detailed in the previous restriction requirement mailed July 19, 2006, a search of one sequence would not necessarily reveal art against a different sequence.

Applicants also argue that the sequence of the fragment of the human cardiac α-actin promoter (SEQ ID NO:9) was known prior to this application and is only part of the invention in conjunction with SEQ ID NOs: 2-7. Applicants contend that a search of the prior art for SEQ ID NOs: 2-7 would also reveal if any of these CARP sequences were used in conjucntion with a fragment of the human cardiac α-actin promoter.

This argument and contention has been fully considered but is not found persuasive because regardless of the fact that SEQ ID NO:9 was known prior to this application, as discussed above, a search of each of the sequences represented by SEQ ID NOs: 2-7 would not necesarrily reveal art against each other. Therefore, it would be unduly burdensome to search the sequences of SEQ ID NOs: 2-7 independently, or in conjucntion with SEQ ID NO:9 in one application.

In summary, the polynucleotides of SEQ ID NO:2-7 and SEQ ID NO:9 are different molecules with different chemical and physical structures so that independent searches of the prior art would be required that would constitute a serious burden on the Examiner. A search of one SEQ ID NO. would not necessarily reveal art against

another SEQ ID NO. The search and examination of SEQ ID NOs: 2-7 and SEQ ID NO:9 in one application would require a separate and independent search for each sequence. A search of each independent and unique sequence represented by SEQ ID NOs: 2-7 and SEQ ID NO:9 constitute a serious search burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-6, 8, 20, 21, and SEQ ID NOs. 2, 4-7, 9, and a polynucleotide comprising a fragment of SEQ DI NO:2 or a fragment having at least 80% sequence identity to a fragment of SEQ ID NO:2, wherein said fragment is at least 772 nucleotides are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 8, 2006.

Claims 1, 2, 7, 9-19, and SEQ ID NO:3 have been examined on the merits.

Information Disclosure Statement

Applicant's information disclosure statement filed August 30, 2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Priority

Applicant's reference to priority in the first sentence of the specification is acknowledged. However, the instant invention has been afforded priority to March 17, 2004, which is the filing date of the instant application because support for claims drawn to a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide is not found in any application for which Applicants claim priority to.

In summary, the claimed invention has been afforded priority to March 17, 2004, which is the filing date of the instant application because parent applications for which Applicants claim benefit to do not have support for a polynucleotide comprising a fragment of **SEQ ID NO:3**, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. More specifically, SEQ ID NO:3, which is 2,740 nucleobases in length, is not found in any parent application(s). If Applicants believe that they are entitled to an earlier priority date, the Examiner urges Applicant to specifically point where support can be found for the invention drawn to a polynucleotide comprising a fragment of **SEQ ID NO:3** in any applications Applicants claim priority to.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 7, 9-19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 2, 7, 9-19, recite the term "polynucleotide". The instant specification does not define the term "polynucleotide", however page 5, [014] recites "the invention relates to any polynucleotide of natural origin". The instant specification at page 5 [015] further recites, "polynucleotide of natural origin" is understood to mean a genomic DNA fragment". Given this disclosure, the term "polynucleotide" recited in the claims reads upon a naturally occurring polynucleotide, which is a product of nature that does not clearly show the "hand of man". Language at the beginning of these claims such as "an isolated polynucleotide" would overcome the instant rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11 and 13 are indefinite because they recite the limitation, "wherein the protein of therapeutic interest" in line 2 of each claim. There is insufficient antecedent basis for this limitation in the claims because claim 9 from which claims 11 and 13 depends therein recites, "a protein or an RNA of therapeutic interest". Replacing the claims with the limitation, "wherein the protein or an RNA of therapeutic interest" would overcome the instant rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 7, 9-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant invention is drawn to a polynucleotide comprising a fragment of SEQ ID NO:3, or a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. The specification provides an example of a polynucleotide comprising SEQ ID NO:3, or a fragment of SEQ ID NO:3, wherein

said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide (see Examples using SEQ ID NOs: 4-7). However, the claims are so broad to include a polynucleotide comprising a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. The specification as filed fails to adequately describe those polynucleotides comprising a fragment of a sequence that hybridizes under high stringency conditions to SEQ ID NO:3 which retain the function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide as instantly claimed. This functional limitation itself is not sufficient to provide a structure/function relationship for meeting the written description requirement because it is not clear what structure the polynucleotides comprising a fragment of SEQ ID NO:2 or fragments having at least 90% identity to a fragment of SEQ ID NO:2 would have by the recitation of the functionality alone, "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide". The specification provides no guidance in this regard. Apart from further experimentation, the skilled artisan would not have been able to predict the structures of the full scope of the claimed polynucleotides encompassed by the instant invention, particularly in the absence of any teaching by way of structure or reference to active domains or regions. The claimed invention as a whole is not adequately described if the claims require

essential or critical elements which are not adequately described in the specification. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff vs. Electronics, Inc.*, 48 USPQ2d, 1641, 1646 (1998).

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp. 71427-71440.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invention what is claimed." (See Vas-Cath at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a polynucleotide comprising SEQ ID NO:3, or a fragment of SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene

which is operably linked to said polynucleotide meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7, and 9-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. WO0246220.

Claims 1 and 2 are drawn to a polynucleotide comprising a fragment of SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. Claims 7 and 9-19 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the polynucleotide further comprises an expression cassette comprising a sequence encoding a protein or RNA of therapeutic interest; wherein the protein or RNA of therapeutic interest increases a rate of cardiac cell division or reduces or suppresses an immune response; wherein the protein or RNA of therapeutic interest is a vascular

endothelial growth factor or an immunosuppressive protein, including IL-10; wherein the protein or RNA of therapeutic interest reduces hypoxia; wherein the polynucleotide further comprises a vector, wherein the vector comprises an origin of replication; wherein the vector is a plasmid which is derived from adenovirus; and a composition comprising a therapeutically effective amount of the vector comprising said polynucleotide and a pharmaceutically-acceptable carrier.

It is noted that the instant specification does not define the term, "fragment". Applicant is reminded that that during patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See MPEP § 2111-2116.01. Given its broadest reasonable interpretation, the Examiner has interpreted the term, "fragment" to simply include a fragment of greater than 20 bp of SEQ ID NO:3.

Schwartz et al. WO0246220 disclose and claim a polynucleotide comprising a fragment of a sequence of the mouse CARP protein (SEQ ID NO:1), wherein said polynucleotide specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide (see Schwartz et al. claim 1). The Examiner would like to stress that the claims of the instant invention are so broad to include a polynucleotide comprising a **fragment** of SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. It is noted that SEQ ID NO:1 disclosed by Schwartz et al. WO0246220 has 80% overall sequence identity with SEQ ID NO:3 of the instant invention and represents a "fragment" of SEQ ID NO:3. In fact, SEQ ID NO:1 disclosed by Schwartz

et al. WO0246220 is replete with fragments of SEQ ID NO:3. For example, the Examiner has performed a Blast sequence alignment of SEQ ID NO:3 of the instant invention with that of SEQ ID NO:1 disclosed by Schwartz et al. WO0246220 and the results show that that Schwartz et al. SEQ ID NO:1 comprises several fragments of SEQ ID NO:3 (see attached Blast 2 Sequences #3). Particularly, compare Query (Sequence 1, which is SEQ ID NO:3 of the instant invention) at nucleobases -2087 to -2116 and -2569 to -2598 with Sbjct (Sequence 2, which is SEQ ID NO:1 disclosed by Schwartz et al. WO0246220) at nucleobases -1653 to -1682 and -2135 to -2164, respectively. Schwartz et al. also disclose and claim the polynucleotide of their invention further comprises an expression cassette comprising a sequence encoding a protein or RNA of therapeutic interest (see claim 4). Schwartz et al. also disclose and claim wherein the protein or RNA of therapeutic interest increases a rate of cardiac cell division or reduces or suppresses an immune response (see claim 6). Schwartz et al. also disclose and claim wherein the protein or RNA of therapeutic interest of their invention is a vascular endothelial growth factor or an immunosuppressive protein, including IL-10 (see claims 7 and 9). Schwartz et al. also disclose and claim wherein the protein or RNA of therapeutic interest reduces hypoxia (see claim 11). Schwartz et al. also disclose and claim wherein the polynucleotide further comprises a vector and the vector comprises an origin of replication (see claims 12 and 14). Schwartz et al. also disclose and claim wherein the vector is a plasmid which is derived from adenovirus (see claim 16). And finally, Schwartz et al. also disclose and claim a composition comprising a therapeutically effective amount of the vector comprising said

polynucleotide of their invention and a pharmaceutically-acceptable carrier (see claim 20).

Therefore, Schwartz et al. WO0246220 anticipate claims 1, 2, 7, and 9-19.

Claims 1, 2, 7, 15, 17, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuo et al. (Development, 1999 Vol. 126:4223-4234, made of record on the information disclosure statement filed August 30, 2004).

The claims are as described above in the 35 U.S.C. 102(b) rejection against claims 1, 2, 7, and 9-19 as being anticipated by Schwartz et al. WO0246220. Applicant is also reminded of the Examiner's interpretation of the term, "fragment".

Kuo et al. disclose the cloning of a 10 Kb fragment of the mouse CARP gene and the sequencing of a 2.5 Kb fragment upstream of the coding sequence. Kuo et al. disclose deletions from the 5'-end of the fragment were made and showed that a region of 213 bp of the promoter between nucleotides -166 and +47, relative to the transcription start position +1, was sufficient to confer cardiospecific expression, which suggested the presence, at the 5'-end, of an element for controlling the specificity of the promoter (see Figure 3C). Specifically, Kuo et al. disclose the cardiac expression of a specific construct, namely p0.295Luc (-295 to +47). More specifically, Kuo et al. disclose, regarding construct p0.295luc, "expression of the transgene was specific to both the myocardium of the heart and the somites, and cardiac expression was first detected at around E9.95. Cardiac expression of the transgene was restricted to the conotruncal and right ventricular segments of the primitive heart" (see page 4227, first

column, last paragraph, and Figures 4D, H, and 5C).

The Examiner would like to stress that the claims of the instant invention are so broad to include a polynucleotide comprising a **fragment** of SEQ ID NO:3, wherein said polynucleotide, in the absence of inverted terminal repeat sequences from AAV, specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said polynucleotide. It is noted that construct p0.295Luc (-295 to +47) disclosed by Kuo et al. has 82% overall sequence identity with SEQ ID NO:3 of the instant invention and represents a "fragment" of SEQ ID NO:3. In fact, construct p0.295Luc is replete with fragments of SEQ ID NO:3. For example, the Examiner has performed a Blast sequence alignment of SEQ ID NO:3 of the instant invention with construct p0.295Luc disclosed by Kuo et al. and the results show that construct p0.295Luc comprises several fragments of SEQ ID NO:3 (see attached Blast 2 Sequences #1). For example, see the attached Blast 2 Sequence Results and compare Sequence 1 (SEQ ID NO:3 of the instant invention) with Sequence 2 (construct p0.295Luc). Particularly, compare Query (Sequence 1) at nucleobases -2489 to -2512 and -2569 to -2598 with Sbjct (Sequence 2) at nucleobases -89 to -112 and -164 to -193, respectively. It is noted that Kuo et al. disclose that the CARP constructs were transfected into cells via the calcium phosphate method of transfection, where calcium phosphate represents a pharmaceutically-acceptable carrier.

Therefore, Kuo et al. anticipate claims 1, 2, 7, 15, 17, and 19.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by

Aihara et al. (GenBank Accession Number AF131884, made of record on the information disclosure statement filed August 30, 2004).

The claims are as described above in the 35 U.S.C. 102(b) rejection against claims 1, 2, 7, and 9-19 as being anticipated by Schwartz et al. WO0246220. Applicant is also reminded of the Examiner's interpretation of the term, "fragment".

Aihara et al. disclose a 2074 bp sequence fragment of the human CARP promoter. It is noted that this sequence shares 98% overall sequence identity with SEQ ID NO:3 of the instant invention (see attached Blast 2 Sequences #2, where Sequence 1/Query is SEQ ID NO:3 of the instant invention and Sequence 2/Sbjct is Aihara et al., GenBank Accession Number AF131884). Further, it is noted that the sequence disclosed by Aihara et al. is replete with is replete with fragments of SEQ ID NO:3 (see attached Blast 2 Sequence results for explanation).

The burden of establishing whether the prior art human CARP promoter fragment has the further function of specifically inducing expression in cardiac cells *in vivo* of a gene which is operably linked to said fragment under generally any assay conditions as instantly claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its

fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that prior art human CARP promoter fragment disclosed by Aihara et al. would or would not have the additional functional limitation of "specifically induces expression in cardiac cells *in vivo* of a gene which is operably linked to said fragment" under generally any assay conditions.

Therefore, absent evidence to the contrary, claims 1 and 2 are anticipated by Aihara, et al.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
September 27, 2006